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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,542	03/04/2002	Nikolay V. Kuchuk	ICON-001	5528
530	7590	02/25/2005	EXAMINER	
LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK 600 SOUTH AVENUE WEST WESTFIELD, NJ 07090			HELMER, GEORGIA L	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,542	KUCHUK ET AL.	
	Examiner	Art Unit	
	Georgia L. Helmer	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 12 November 2004.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 4-15, 17-32 and 36 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-3, 16 and 33-35 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>Nov2001, Nov2004</u> .	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of Applicant's restriction election, 12 November 2004. Applicant elects Species [m] , claims 1-3, 16 and 33-35, with traverse. Applicant traverses, stating that no lack of unity was made in the International Preliminary Examination Report in connection with the same claims that were present in the corresponding PCT application, and that full faith and credit should be given to the search and action of a previous Examiner. Applicant further traverses Examiner's citation that the instant claims lack unity over Hadley. Applicant's traversal is unpersuasive. Each Examiner sees cases differently. Art becomes available that was not available previously. The instant invention lacks unity of invention over WO 01/85969, entitled Genetic transformation in Plants using site-specific recombinase and wide hybridization.

Claims 1-36 are pending. Claims 1-3, 16 and 33-35, drawn to *Pennisetum* as the first plant and wheat as the second plant, are examined in this action. Claims 1-15 and 17-36 as drawn to other than *Pennisetum* as the first plant and wheat as the second plant are withdrawn as being drawn to non-elected inventions. This restriction is made FINAL.

Information Disclosure Statement

2. Initialed and dated copies of Applicant's IDS form 1449, filed 26 November 2004 and 15 November 2001, respectively, are attached to the instant Office action.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34 and 35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 34 and 35 are drawn to seed, seed parts or progeny from the whole plant containing a heterologous nucleic acid. Since the plants and plant material have not been raised under selective conditions, some of the plant material will not be transgenic, rather it will be wild-type, which is a product of nature. Progeny of wild-type tissue are wild-type. Furthermore, due to Mendelian segregation of the transgene, even some progeny of transformed Allium will not retain the transgene. See American Wood v. Fiber Disintegrating Co., 90 U.S. 566 (1974), American Fruit Growers v. Brogdex Co., 283 U.S. 2 (1931), Funk Brothers Seed Co. v. Kalo Inoculant Co., 33 U.S. 127 (1948), Diamond v. Chakrabarty, 206 USPQ 193 (1980)

Claim Rejections - 35 USC § 112-second

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-3, 16 and 33-35 are rejected under 35 U.S.C. 112-2nd.

Claims 1-3, 16 and 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: formation of a hybrid cell of a first plant and a second plant, chromosome pairing and recombination occurring between chromosomes of the first plant and the second plant in such a manner as to produce recombination at recombination sites and insert a nucleotide sequence of interest into the genome of the second plant, production of haploid cell, culturing of cell(s)/tissue to produce a hybrid transgenic plant.

Claim Rejections - 35 USC § 112-Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 16 and 33-35, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's claims are drawn to a method of introducing genetic material into plants by preparing a first plant transformed with a heterologous nucleic acid having a 5' and 3' excisable flanking sequence that allow movement of said heterologous nucleic acid from one genome to another, crossing a second plant

and the transformed first plant, wherein said first and second plants, upon crossing produce unstable progeny or demonstrate preferential segregation or sorting out; wherein the excisable flanking sequence comprise a transposable element and the first and second plant produce the compatible transposases, and wherein the excisable flanking sequence comprise a recombination site and the first and second plant produce the compatible recombinase, wherein *Pennisetum* as the first plant and wheat as the second plant,

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

Re the nature of the invention and the breadth of the claims:
Applicant's invention is a method of introducing genetic material into plants by preparing a first plant transformed with a heterologous nucleic acid having a 5' and 3' excisable flanking sequence that allow movement of said heterologous nucleic acid from one genome to another, crossing a second plant and the

transformed first plant, wherein said first and second plants, upon crossing produce unstable progeny or demonstrate preferential segregation or sorting out; wherein the excisable flanking sequence comprise a transposable element and the first and second plant produce the compatible transposases, and wherein the excisable flanking sequence comprise a recombination site and the first and second plant produce the compatible recombinase.

Re the amount of guidance given, and the presence of working examples:

Applicant gives 5 examples (specification, p. 15-18):

"Example I, Transformation /line conversion of Brassica napus" using Orychophragmus violaceous as the first plant and Brassica species as the second plant, including description of transformation constructs comprising the Spm transposase and related elements .

"Example II, Transformation /line conversion of Brassica napus" using Arabidopsis thaliana as the first plant and Brassica species as the second plant .

"Example III, Transformation /line conversion of potato" using Arabidopsis thaliana as the first plant and Potato as the second plant.

"Example IV, Transformation /line conversion of maize" using Tripsacum dactyloides as the first plant and maize as the second plant.

"Example V, Transformation /line conversion of wheat", for which no information is given, other than a reference to how the crosses were done. The first plant is not identified.

Each of these Examples includes only very rudimentary experimental details and closes with statements to the effect that the transformation was

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done, crosses were done, and progeny were selected. No details of what, if any, of the examples produced any of the desired progeny, having the desired heterologous nucleic acid transferred from the first plant to the second plant.

No examples are given of the transformation /line conversion wherein Pennisetum as the first plant and wheat as the second plant. No information is given on any of the putative Spm transformants and related heterologous nucleic acid transferred. No examples are given of any recombinase, wherein the excisable flanking sequence comprise a recombination site and the first and second plant produce the compatible recombinase. The claimed invention is not exemplified.

The predictability of the art or lack thereof:

Re sexually crossing any plant, where plants are of different species:
Applicant claims the transformation /line conversion wherein Pennisetum as the first plant and wheat as the second plant. Applicant indicates an Example wherein wheat is the second plant (specification p. 15-18) but gives no details, no information on the identity of the first plant, which is the other parent in the wide hybridization cross, and gives no information on which, if any, of the progeny produce the claimed transgenic progeny. Species are groups of potentially interbreeding natural populations which are reproductively isolated from other such groups (Rieger et al., Glossary of Genetics & Cytogenetics, 1976, Springer-Verlag, NY, page 511). The state of the art is that such at one skilled in the art can readily do sexual crosses within the species, with reasonable expectation of success of hybrid progeny. However, the interspecific cross is difficult to make

and the hybrid that is produced is often inviable or sterile (Hadley et. al., in Hybridization in Crop Plants, ed. Fehr & Hadley, Society of Agronomy and Crop Science Society of America, Madison, Wisconsin, page 133). Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden. Without further guidance, one of skill in the art would be required to do many experiments involving a myriad of combinations. This would impose a burden on the skilled artesian, without a reasonable expectation of success.

Re the recombinase: Applicant claims all recombinases, and use of all recombinases in the claimed invention. Applicant gives no information or guidance with respect to the use of the specific recombinase system. Site-specific recombinase are very complex enzyme systems where the recombinase has several functions—namely, recognition of recombination sites, cleavage of recombination site at specific cleavage sites, strand swapping to produce the recombinant strand, and ligation to produce the reconfigured product. It is unpredictable that any recombinase, would properly perform all the above functions. Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden. Without further guidance, one of skill in the art would be required to do many experiments involving a myriad of combinations. This would impose a burden on the skilled artesian, without a reasonable expectation of success.

Re generation a haploid transgenic plant. This process needs to have had the following events occur successfully and in the proper sequence for such generation:

- Sexual crossing
- providing the recombinase,
- generating a haploid plant.

For formation of a hybrid cell of acceptor plant and donor plant, chromosome pairing and recombination occurring between chromosomes of donor plant and acceptor plant in such a manner as to produce recombination at non-identical sites and insert nucleotide sequence of interest at target site, production of haploid cell, culturing of cell(s)/tissue to produce a hybrid transgenic plant. A number of issues need to be addressed successfully for this process to occur: synthesis of the hybrid, chromosome pairing and genetic recombination. Of issue in wheat/maize hybridization, are crossibility of the parents, and specific genotypes of the parents to be used, among other factors, as discussed by Jauhar, et. al. Chromosome-mediated and direct gene transfers in wheat, Genome 42: 570-583, 1999, pages 572-3.

The chromosomes need to pair and recombination occur to produce the desired product. Recombination occurs upon such time as the recombinase is provided and catalyses the various recombinase events. The recombinase needs to be provided at the proper time, in the proper place , at an adequate concentration, at the proper phase of the cell cycle, for the proper duration of

time for the desired recombination event(s) to occur. For the site-specific recombinases, the recombination event is reversible. Since the wild-type recombination sites readily recombine with each, the proper conditions for catalysis need to be determined for the successful event to occur. Embryo rescue is necessary for haploid production from wheat x maize hybrids (Zhang, et. al., Wheat embryogenesis and haploid production in wheat x maize hybrids, Euphytica 90: 315-324, 1996, p 315.). Proper conditions for this need to be determined. Once transgenic haploid cell(s) are produced, they need to be regenerated into the transgenic haploid plants.

While working examples are not required, Applicant must provide sufficient guidance to address these issues discussed above. Without such guidance, the experimentation required would not be routine, but would be undue. Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden. Without further guidance, one of skill in the art would be required to do many experiments involving a myriad of combinations. This would impose a burden on the skilled artisan, without a reasonable expectation of success.

Experimentation required: Undue experimentation would be required to determine which **combinations and sequence of the various steps** would function to produce the claimed invention. For example, what recombinase, of the many available such as the site-specific recombinases systems FLP/FRT, Cre/lox, R/Rx would function as desired for the movement of a heterologous

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nucleic acid from a chromosome of one genome of one species to a chromosome of the genome of a second species. The recombinase needs to be provided at the proper time, in the proper place , at an adequate concentration, at the proper phase of the cell cycle, for the proper duration of time for the desired recombination event(s) to occur. Determining the specific combinations and sequences of the various steps which would function to produce the claimed invention would require a number of independent sets of experimentation.

Experimentation would need to determine which recombinases, in which parental plants, in what transgenic construct, with what kind of regulatory sequences for expression of the recombination partners, be such expression sequence tissue specific, cell cycle dependent, or developmental stage specific, would function to produce the claimed invention. There are an infinitely large number of combinations of regulatory sequences for coding sequences and a number of possible recombinases; these factors alone would require an exceeding large number of sets of experiments to determine which ones would function as desired. Applicant must provide sufficient guidance to address these issues. Without such guidance the experimentation required would not be routine, but would be undue. This would impose a burden on the skilled artesian, without a reasonable expectation of success.

In view of the breadth of the claims (sexually crossing any plants from different species, any recombinase, any Pennisetum of any genotype at any age grown in any soil under what kind of growth conditions, any wheat plant of any genotype) and the lack of guidance in the specification, undue experimentation would be required to enable the invention as commensurate in scope with the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Remarks

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 571-272-0796. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Georgia Helmer PhD
Patent Examiner
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February 15, 2005



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